

## **REMARKS**

### **Formal Matters**

Claims 1, 2, 6, 8, 9, 12-15, 21, 25, 26, 69, 74, and 80 are pending in this application. Claims 1, 6, 69, 74, and 80 are amended merely to change claim dependency, correct inadvertent typographical errors, or to narrow the issues on appeal should an appeal become necessary.. Support for the amendments is found in the previously presented claims. No new matter is added by the amendments. The examiner is respectfully requested to enter the amendments.

Claims 3-5, 7, 10, 11, 16-20, 22-24, 27-68, 70-73, 75-79 are canceled or withdrawn due to earlier restriction requirements. Amendment, withdrawal or cancellation of claims is done without prejudice to later prosecution and is done merely to expedite prosecution and allowance of the claims or to narrow the issues on appeal should an appeal become necessary.

### **Claim Rejections**

Applicants note that claims 11 and 69 are not rejected in the Office Action, although they are listed among the rejected claims in the Office Action Summary. Applicants respectfully request allowance of claims 11 and 69 as encompassing allowable subject matter. If, on the other hand, the claims are rejected under one of the rejections in the Office Action, Applicants consider the arguments below to support withdrawal of the rejections of claims 11 and 69 just as for the other claims.

### **Rejection under 35 USC § 102(b) (Alderson et al.)**

Claims 1, 2, 4, 8, 9, and 12-15 remain rejected under 35 USC 102(b) as allegedly being anticipated by Alderson et al. (1994, International Immunology, vol. 6, pages 1799-1806). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The pending claims are drawn to an isolated antibody which is not a native IgM or IgA antibody, the isolated antibody comprising an Fc region and three or more antigen binding sites amino-terminal to the Fc region comprising at least one polypeptide chain

with the formula: (a) VH-CH1-flexible linker-VH-CH1-Fc region chain, wherein the flexible linker comprises the peptide gly-ser-gly-ser (SEQ ID NO:10).

Alderson et al. discloses an anti-Fas IgM antibody. The pending claims are drawn to an isolated antibody which is not a native IgM or IgA antibody. As a result, the pending claims are anticipated by Alderson et al. under 35 USC 102(b). Withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 103(a) (Zapata et al. and Shu et al.)

Claims 1, 2, 4-9, 12-15, 57-68, and 74-78 are rejected under 35 USC 103(a) as allegedly being unpatentable over Zapata et al. (1995, Protein Engineering, vol. 8, pages 1057-62, primary reference) in view of Shu et al. (1993, PNAS USA, vol. 90, pages 7995-7999). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The pending claims are drawn to an isolated antibody which is not a native IgM or IgA antibody, the isolated antibody comprising an Fc region and three or more antigen binding sites amino-terminal to the Fc region comprising at least one polypeptide chain with the formula: (a) VH-CH1-flexible linker-VH-CH1-Fc region chain, wherein the flexible linker comprises the peptide gly-ser-gly-ser (SEQ ID NO:10).

Neither Zapata et al. nor Shu et al. disclose an isolated antibody as claimed by Applicants in which VH-CH1 domains are linked by a gly-ser-gly-ser flexible linker. The combination of Zapata et al. and Shu et al. does not cure the deficiency of either reference alone. As a result, the combination of Zapata et al. and Shu et al. does not render Applicants' invention obvious in view of the combined references. Withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 103(a) (Zapata et al., Shu et al. and WO 98/41629)

Claims 1, 2, 4-9, 12-15, 21, 25, 26, 33-37, 41, 42, 57-66, 68 and 74-78 remain rejected under 35 USC 103(a) as allegedly being unpatentable over Zapata et al. (*supra*) in view of Shu et al. (*supra*), and further in view of WO 98/41629 (IDS, September 24, 1998). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The pending claims are drawn to an isolated antibody which is not a native IgM or IgA antibody, the isolated antibody comprising an Fc region and three or more antigen binding sites amino-terminal to the Fc region comprising at least one polypeptide chain with the formula: (a) VH-CH1-flexible linker-VH-CH1-Fc region chain, wherein the flexible linker comprises the peptide gly-ser-gly-ser (SEQ ID NO:10).

The combination of Zapata et al. and Shu et al. as failing to yield Applicants' invention is discussed above and applies to the rejection of claims 1, 2, 4-9, 12-15, 21, 25, 26, 33-37, 41, 42, 57-66, 68 and 74-78. The addition of WO 98/41629 does not cure the deficiency of the combination of Zapata et al. and Shu et al. WO 98/41629 discloses DR5, the antigen species elected by Applicants. WO 98/41629 does not disclose an isolated antibody as claimed by Applicants in which VH-CH1 domains are linked by a gly-ser-gly-ser flexible linker. The combination of Zapata et al., Shu et al. and WO 98/41629 does not cure the deficiency and does not render Applicants' invention obvious in view of the combined references. Withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 103(a) (Zapata et al., Shu et al. and Paprocka et al.)

Claims 66, 75, and 80 remain rejected under 35 USC 103(a) as allegedly being unpatentable over Zapata et al. (*supra*) in view of Shu et al. (*supra*), and further in view of Paprocka et al. (1992, Arch Immunol. Ther Exp., vol. 40, pages 223-227, abstract only). Applicants respectfully traverse the rejection as applied and as it might be applied to the currently pending claims for the reasons provided below.

The pending claims are drawn to an isolated antibody which is not a native IgM or IgA antibody, the isolated antibody comprising an Fc region and three or more antigen binding sites amino-terminal to the Fc region comprising at least one polypeptide chain with the formula: (a) VH-CH1-flexible linker-VH-CH1-Fc region chain, wherein the flexible linker comprises the peptide gly-ser-gly-ser (SEQ ID NO:10).

The combination of Zapata et al. and Shu et al. as failing to yield Applicants' invention is discussed above and applies to the rejection of claims 66, 75, and 80. The addition of Paprocka et al. does not cure the deficiency of the combination of Zapata et al. and Shu et al. Paprocka et al. disclose linking the cytotoxic agent, ricin, to a

monoclonal antibody. Paprocka et al. do not disclose an isolated antibody as claimed by Applicants in which VH-CH1 domains are linked by a gly-ser-gly-ser flexible linker. The combination of Zapata et al., Shu et al. and Paprocka et al. does not cure the deficiency and does not render Applicants' invention obvious in view of the combined references. Withdrawal of the rejection is respectfully requested.

SUMMARY

Claims 1, 2, 6, 8, 9, 12-15, 21, 25, 26, 69, 74, and 80 are pending in this application. Claims 1, 6, 69, 74, and 80 are amended. The examiner is respectfully requested to enter the amendments.

Claims 3-5, 7, 10, 11, 16-20, 22-24, 27-68, 70-73, 75-79 are canceled or withdrawn due to earlier restriction requirements. Amendment, withdrawal or cancellation of claims is done without prejudice to later prosecution and is done merely to expedite prosecution and allowance of the claims or to narrow the issues on appeal should an appeal become necessary.

Applicants note that claims 11 and 69 were not rejected in the Office Action and request allowance of these claims as containing allowable subject matter.

Applicants have overcome the rejections under Section s 102(b) and 103(a). Withdrawal of the rejections and allowance of the claims is respectfully requested.

If in the opinion of the Examiner, a **telephone conference** would expedite the prosecution of the subject application, the Examiner is **strongly encouraged** to call the undersigned at the number indicated below.

This response/amendment is submitted with a transmittal letter and petition for a three-month extension of time and fees. In the unlikely event that this document is separated from the transmittal letter or if fees are required, applicants petition the Commissioner to authorize charging our Deposit Account 07-0630 for any fees required or credits due and any extensions of time necessary to maintain the pendency of this application.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Respectfully submitted,

GENENTECH, INC.

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By 

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